having the ability to bind a nucleic acid. The idea is to prepare a peptide that can bind to DNA without changing the peptide's properties. After binding to the nucleic acid, the conjugate is introduced into cells that use the particular property of the biologically active peptide, thereby carrying out gene transfer therapy.

Weiner et al expresses an HCV polypeptide by genetic engineering techniques and uses the simple peptide in immunoassays.

The Takahara et al method of gene transfer would not have suggested performing any immunoassay, particularly on a nucleaic-acid bound peptide. The Examiner has merely cited a reference that suggests binding a protein to a DNA for a completely unrelated purpose, together with a reference describing an immunoassay. That does not establish a *prima facie* case of obviousness.

The basic idea of the present invention is to intentionally change the performance of the peptide in an immunoassay so as to increase the immunological reactivity of the peptide, by using a nucleic acid. The reason for combining the peptide and DNA, as well as the nature of the claimed method, are utterly different from those of Takahara et al in which the properties of the biologically-active peptide are not changed and the purpose is gene therapy. Weiner et al also does not involve changing the properties of the peptide.

The Examiner asserts that we criticized the obviousness rejection on grounds that Wiener et al. does not indicate what would happen to the antigenic properties of the polypeptide (Official Action page 3, lines 10-15). However, that is not what we argued. The obviousness rejection should be withdrawn because nothing in the references gives any reason to do an immunoassay with a nucleic acid-bound polypeptide as the substrate. We did however, argue that a person of skill in the art who had thought of doing such an assay would

be very concerned about the DNA having a negative effect on the antigenicity of the peptide. But the references provide no guidance on that point.

Comparative data in the specification demonstrates unexpected properties in the invention. Table 2, on page 29, shows that the HCV-positive serum could only be detected when the polypeptide/nucleic acid conjugate (120 NA(+)) was fixed on gelatin particles. Therefore, the antigenic properties of the polypeptide to the antibody were increased by binding the nucleic acid to the polypeptide. This increase in assay sensitivity was totally unexpected in view of Takahara et al and Weiner et al.

Applicants submit that the case is now in condition for allowance. Early notification of such action is earnestly solicited.

Respectfully submitted,

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